Supplemental Video 1. Interkinetic nuclear migration in cerebral organoids. Live imaging of GFP electroporated organoid revealing movement of nuclei along apical and basal processes of RG. Arrow marks one RG in particular with clear IKNM. Time shown in hrs:min.

Supplemental Video 2. Calcium surges in neurons of cerebral organoids. Live imaging of Fluo-4 signal in a human cerebral organoid revealing spontaneous calcium surges in individual neurons (arrows). Time shown in min:sec.

Supplemental Video 3. False color heat map of spontaneous neural activity. False color heat map of a zoomed in region of Supplemental Video 2 showing spontaneous calcium surges. Time shown in min:sec.

Supplementary Text

Patient clinical synopsis. Patient A3842 exhibited growth restriction from fetal life, with marked reduction in brain size evident at 22/40 weeks gestation. Pregnancy progressed otherwise normally and the patient was born at term weighing 1.82kg (-3.9 s.d.). Postnatally, growth was also reduced such that height at 3 years 7 months was 73 cm (-6.7 s.d.), and head circumference 35cm (-13.2 s.d.), in keeping with a severe disproportionate microcephaly. The patient had quite prominent eyes and conical shaped wide-space teeth, but was otherwise unremarkable on examination. No neurological deficits or malformations in other systems were evident, aside from a mixed conductive/sensorineural hearing loss. Development milestones were mildly/moderately delayed. Neuroimaging at 22/40 gestation demonstrated a smooth brain (the Sylvian fissure normally evident at this gestation was not present) with small frontal lobes and partial absence of the corpus callosum. Postnatally, MRI demonstrated microcephaly with a simplified gyral pattern and a cerebral cortex of normal thickness. In summary, clinical findings were in keeping with previous cases of CDK5RAP2 primary microcephaly (deafness has been previously reported with CDK5RAP2[45,46]), with growth parameters falling on the primary microcephaly-microcephalic primordial dwarfism spectrum reported for other centrosomal microcephaly genes such as *CENPJ* and *CEP152*[45,54-56].